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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/551,466	08/07/2006	Ji Hoon Jeong	2236.0180000/JUK/SMW	4435

26111 7590 01/08/2008

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EXAMINER	
PITRAK, JENNIFER S	

ART UNIT	PAPER NUMBER
1635	

MAIL DATE	DELIVERY MODE
01/08/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/551,466	JEONG ET AL.	
	Examiner	Art Unit	
	Jennifer Pitrak	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 November 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-13* is/are pending in the application.

4a) Of the above claim(s) *9-13* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *12/21/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group I, claims 1-8, in the reply filed on 11/15/07 is acknowledged. The traversal is on the ground(s) that the inventions of Groups I, II, and VI are related as subcombination-combination and would not present an undue search burden on the Office. This is not found persuasive because according to 37 CFR 1.475(b) as stated in the Restriction/Election requirement mailed 10/15/07, the claims do not fall into any one of the only 5 combinations of categories considered to have unity of invention (see bottom of p.2 to p.3 of Restriction Requirement mailed 10/15/07). The requirement is still deemed proper and is therefore made FINAL.

Applicants noted that the Examiner failed to include claim 14 in any of Groups I-IV in the Restriction Requirement mailed 10/15/07 and requested that the Examiner clarify the Restriction Requirement to include claim 14. However, the Interview Summary dated 10/15/07 indicated that the claim set having claims 1-13 and filed on 10/03/05 is the pending claim set and that claim 14 has been cancelled. Thus, the restriction requirement should only include claims 1-13.

Applicant's election with traverse of polyethylene glycol from claim 4 in the reply filed on 11/15/07 is acknowledged. The traversal is on the ground(s) that all species listed in claims 4-8 have a common property and/or activity. Applicants specifically indicate that the species listed in claim 4 (polyethylene glycol, polyvinylpyrrolidone, and polyoxaline) "share common

properties and each member can be substituted one for the other with the expectation that the same intended result would be achieved." This is found persuasive for the species of claim 4.

Applicant's election with traverse of an acid-cleavable linkage from claim 5, a phosphodiester bond from claim 6, an antisense oligonucleotide from claim 7, and *c-myb* from claim 8 in the reply filed on 11/15/07 is acknowledged. The traversal is on the ground(s) that all species have a common property and/or activity. This not found persuasive because while the species may have a common property or activity, as argued by Applicants, they lack unity of invention because they do not contribute over the prior art as evidenced by the 35 U.S.C. §102 and §103 rejections that follow. The requirement is still deemed proper and is therefore made FINAL.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 8 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claim is to an antisense oligonucleotide comprising part of or the entire *c-myb* gene sequence. As disclosed in the instant specification (page 3, lines 10-12), antisense oligonucleotides are complementary to their target sequence. Thus, claim 8 is indefinite because it claims an antisense oligonucleotide comprising the target sequence and not the complement of the target sequence.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-7 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Tullis (1990, US Patent 4,904,582).

The claims are to a conjugate for gene transfer comprising an oligonucleotide intended to be transferred into a target cell and a hydrophilic polymer (claim 1), wherein the polymer is a non-ionic polymer having a molecular weight greater than 500 daltons and wherein the oligonucleotide has a molecular weight between 1,000 and 50,000 daltons (claims 2 and 3). Claim 4 is to the conjugate of claim 1 wherein the polymer is polyethylene glycol (PEG). Claims 5-7 are to the conjugate wherein the oligonucleotide is an antisense oligonucleotide that is linked to the polymer by an acid-cleavable linkage and wherein the nucleotides are linked by phosphodiester bonds.

Tullis describes oligonucleotide conjugates for transport across cellular membranes for modulating gene expression (abstract). In Table 1 in column 19, Tullis discloses the "MBF 20 antisense C_2-PEG" probe that is antisense to mouse Beta-globin mRNA and comprises a 20-nucleotide phosphodiester-linked molecule connected to PEG (M_r = 3500) by an ester bond, which is disclosed in the instant specification as an acid-cleavable linkage (page 7, lines 7-12). According to the website, www.newton.dep.anl.gov, a 20-nucleotide single-stranded DNA

molecule has a molecular weight of approximately 6600 daltons (330 daltons per nucleotide). Thus, Tullis clearly anticipates the instant claims 1-7.

Claim Rejections - 35 USC § 103

Claim 8 is rejected under 35 U.S.C. 103(a) as being unpatentable over Raschella, *et al.* (1992, Cancer Research, v.52:4221-4226) and Tullis (1990, U.S. Patent 4,904,582).

The claim is to a conjugate for gene transfer comprising a *c-myb*-targeted antisense oligonucleotide covalently linked to a hydrophilic polymer.

Raschella, *et al.* teach *c-myb*-targeted antisense oligonucleotides and inhibition of *c-myb* expression with the antisense oligonucleotides (Fig. 4 and paragraph bridging p.4223-4224). The oligonucleotides were useful for inhibiting growth of tumor cells (abstract and Fig. 6). Raschella, *et al.* do not teach *c-myb* antisense oligonucleotides covalently linked to a hydrophilic polymer.

Tullis teaches oligonucleotides conjugated to PEG as described above (35 USC §102 rejection). Tullis teaches that the oligonucleotide-polymer conjugates are "more efficient in membrane transport, so as to be capable of crossing the membrane and effectively modulating a transcriptional system" (Abstract). At column 2, "Description of the Specific Embodiments", Tullis explains that "the amphiphilic nature of the product [oligonucleotide-polymer conjugates] aids in the transport of the conjugate across the cellular membrane and can provide additional advantages, such as increasing aqueous or liquid solubility of nucleic acid derivatives."

It would have been obvious to make a *c-myb*-targeted antisense oligonucleotide as taught by Raschella, *et al.* conjugated to PEG as taught by Tullis. One would have been motivated to

make the antisense conjugate because Raschella, *et al.* demonstrated that targeting *c-myb* by antisense was useful for inhibiting tumor cell proliferation and Tullis taught that conjugating antisense oligonucleotides to polymers such as PEG provided more efficient transmembrane transport of the oligonucleotides. One would have a reasonable expectation of success in making the conjugates because Tullis demonstrated successful use of such conjugates for targeting the mouse Beta-globin mRNA (see 35 USC §102 rejection above). Thus, the instant claim 8 would have been obvious to one skilled in the art at the time of the instant application.

Closing

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer Pitrak whose telephone number is 571-270-3061. The examiner can normally be reached on Monday-Friday, 8:30AM-5:00PM, EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Schultz can be reached on 571-272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would

like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Jennifer Pitrak
Examiner
Art Unit 1635

Examiner, AU 1635